DIFFERENCES IN THE EPIDEMIOLOGY OF INVASIVE PNEUMOCOCCAL DISEASE, METROPOLITAN NSW, 1997–2001

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Although invasive pneumococcal disease (IPD) accounts for only a minority of the infections caused by *Streptococcus pneumoniae* (such as pneumonia and otitis media), it is associated with the most severe disease and is readily measured, as it is by definition associated with a sterile site isolate.[1] The Metropolitan NSW Pneumococcal Study Group was formed in 1997 to generate data describing the age-specific incidence, serotype distribution and antimicrobial resistance patterns of invasive pneumococcal disease in a large population that is believed to be representative of urban Australia. Results from the first two years of active surveillance for invasive pneumococcal disease in metropolitan NSW have been previously reported.[2] This article presents data from a 4.5-year period, with a greater focus on differences between the regions covered by the area health services within metropolitan NSW. These data provide an expanded picture of the profile of IPD in a representative Australian urban region—the metropolitan area health services within Sydney, the Hunter and the Illawarra.

METHODS

Case definition

Invasive pneumococcal disease was defined as isolation of *S. pneumoniae* from a normally sterile site, including blood, cerebrospinal fluid (CSF), pleural fluid or synovial fluid. Meningitis was defined as isolation of *S. pneumoniae* from CSF; or pneumococcal bacteraemia with abnormal CSF; or, if a lumbar puncture was not performed, evidence of meningitis from imaging or at post-mortem examination. Diagnosis of pneumonia or other focal infection was based on discharge diagnosis and appropriate clinical and radiographical findings. Cases where no focus of infection had been determined at the time of discharge were designated as bacteraemia without focus. Multiple isolates from a single episode of infection were counted only once.

Eligible cases had a postcode of residence within the Sydney, Hunter and Illawarra statistical divisions in the 1996 Census, and a date of collection of the positive specimen between 1 June 1997 and 31 December 2001. The data were then translated into the geographical profile of the metropolitan area health services, to give a profile for metropolitan NSW.

Case ascertainment

Cases were identified from all laboratories within the Sydney, Hunter and Illawarra area health services that process sterile site specimens. Case ascertainment was enhanced through the regular auditing of laboratories and medical record departments for discharge diagnoses coded as pneumococcal meningitis or unspecified bacterial meningitis, pneumococcal septicaemia or pneumococcal pneumonia, according to the International Classification of Diseases. Data on final diagnosis, outcome and underlying conditions, were obtained from review of patient hospital records by a single observer (RG) using a standard protocol. The vaccination status of cases was only available from hospital notes and this source was not thought sufficiently reliable to report.

Antimicrobial susceptibility testing and serotyping

Antimicrobial susceptibility was reported according to the usual practice of the reporting laboratories, all of which participate in the quality assurance program of the Royal College of Pathologists of Australasia. During the study period, the methods used were *E* test (most laboratories),[3] or disc susceptibility testing using the calibrated dichotomous standard (CDS) method.[4] For the first two years of the study, isolates were sent in batches to the Queensland Health Scientific Services for serogrouping and serotyping using reagents from Statens Serum Institute, Denmark. In the remaining years of the study, serogrouping and serotyping for the most common types were established at the microbiology laboratory of The Children's Hospital at Westmead.

Statistical analysis and ethical approval

Statistical analyses were performed using the statistical software SPSS. Incidence was calculated as an annual rate per 100,000 population for the relevant age group, using the annual resident population of the Sydney, Hunter and Illawarra statistical divisions in the 1996 Census.[5] The study was approved by the ethics committees of all the participating hospitals and laboratories. Identifying data were kept secure, with access limited to the principal investigators. Analyses were conducted on de-identified data.

RESULTS

Disease incidence

During the surveillance period 3,033 cases of IPD were identified, of whom 1986 (66 per cent) were adults aged 15 years and over and 1,041 (34 per cent) were children. The age of six cases was unknown; in total, medical records were unavailable for 28 cases (0.9 per cent). Annual incidence was highest at the extremes of age: 102.4 per 100,000 children under the age of two years and 93.5 per 100,000 in people aged 85 years or older.

Among children under the age of two years, IPD was rare under three months (19 cases), and peaked between nine and 20 months, with this age range accounting for 78 per cent of all these cases. The lowest annual incidence (4.1 per 100 000) was between the ages of five and 40 years. The male-to-female ratio was 1.3:1 overall, varying from 1.6:1 in those aged less than 15 years to 0.7:1 among those aged 80 years and over. However, it should be noted that the overall male to female ratio in the latter age group is 0.6 to 1.0.[5]

Seasonality and categories of infection

Invasive pneumococcal disease was clearly seasonal, with 1,017 cases (41 per cent) occurring during the coldest months (June–August), compared with 430 cases (13 per cent) during the warmest months (December–February). Disease manifestations differed between children and adults. Bacteraemia without focus predominated in those less than 15 years of age (680 cases or 66 per cent), while in those aged over 15 years pneumonia was the most common focus of infection (1,516 cases or 77 per cent) (Table 1). Meningitis was most common among children under the age of two years (incidence, 13.1 per 100,000; 95 per cent CI, 10.2–16.0), where it accounted for 13 per cent of cases. Overall, meningitis accounted for seven per cent of cases (incidence, 0.9 per 100,000; 95 per cent CI, 0.8–1.0).

Differences among metropolitan area health services

Figure 1 shows the total incidence of IPD (shown on the left axis) and proportion of cases with a penicillin resistant isolate (shown on the right axis) from lowest to highest, by metropolitan area health service, across all age groups. Figure 2 shows the total incidence of IPD and proportion of cases with a penicillin-resistant isolate from lowest to highest, by health service area, among children less than five years. There was a two-fold difference between the all-age incidence of IPD in the area with the lowest rate (Illawarra, 10.7 per 100,000) and the area with the highest rate (Central Coast, 22.0 per 100,000). Depending on age, however, the rank among the remaining regions differed, with the Central Sydney area in particular having a relatively higher incidence among adults.

Penicillin resistance also varied by age group, health service area and time period. In the two extremes of age (less than five years and 65 years and over) there was a change in resistance patterns between the initial and later parts of the surveillance period. Overall levels of resistance among children under five years have declined from 19 per cent in 1997–99 to 12.5 per cent for 2001, while there has been a slight increase in resistance among adults from 12.5 per cent to 15 per cent. Over the whole period of surveillance, antibiotic resistance remained highest in the South West Sydney area for all age groups. Among children under the age of five years, levels of penicillin resistance were lowest in Northern Sydney while Central Sydney had the lowest levels of resistance among adults (Figures 1 and 2).

Predisposing conditions and mortality

Under current National Health and Medical Research Council recommendations,[6] overall, 54 per cent of cases presented with predisposing illnesses qualifying them for polysaccharide pneumococcal vaccine. This proportion of cases presenting with predisposing illnesses varied significantly with age, from only 12 per cent of children under the age of five years to 86 per cent among those 65 years and over. Of the remaining cases, a further 10 per cent required regular medical review. Among children less than five years of age, the inclusion of those born at less than 28 weeks' gestation (0.9 per cent) or at any gestation with subsequent chronic lung disease (0.7 per cent) or Down's syndrome (0.4 per cent) would increase the proportion of cases with one or more predisposing conditions from 12 to 14 per cent.

Overall, there were 412 deaths (case-fatality rate, 13.6 per cent). The case-fatality rate varied with age and the focus of infection (Figure 3) as well as with underlying illness. Among people with no underlying illness, the case-fatality rate rose from 9/826 (one per cent) in those less than 15 years to 12/304 (four per cent) in those aged

TABLE 1

MANIFESTATIONS OF INVASIVE PNEUMOCOCCAL DISEASE BY AGE, METROPOLITAN NSW, 1997–2001

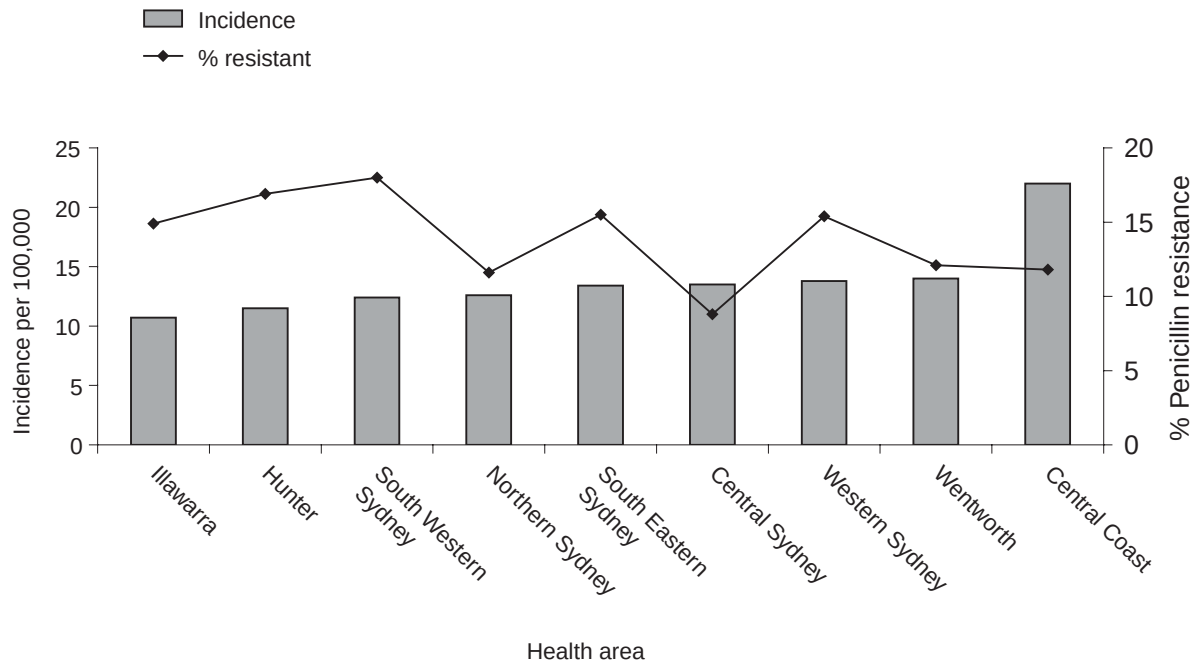
Age (years)	Bacteraemia		Pneumonia		Meningitis		Other focal*		Total
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)	
0–1	405	(66)	94	(15)	79	(13)	39	(6)	617
2–4	216	(68)	79	(25)	17	(5)	7	(2)	319
5–14	59	(59)	31	(31)	7	(7)	3	(3)	100
15–39	57	(15)	291	(77)	23	(6)	5	(1)	376
40–64	89	(18)	342	(71)	45	(9)	6	(1)	482
≥65	172	(16)	883	(80)	34	(3)	16	(1)	1105
Total	**998**	**(33)**	**1720**	**(57)**	**205**	**(7)**	**76**	**(3)**	**2999**

*Other focal diseases included cellulitis, arthritis and epiglottitis.

Source: The Metropolitan NSW Pneumococcal Study.

FIGURE 1

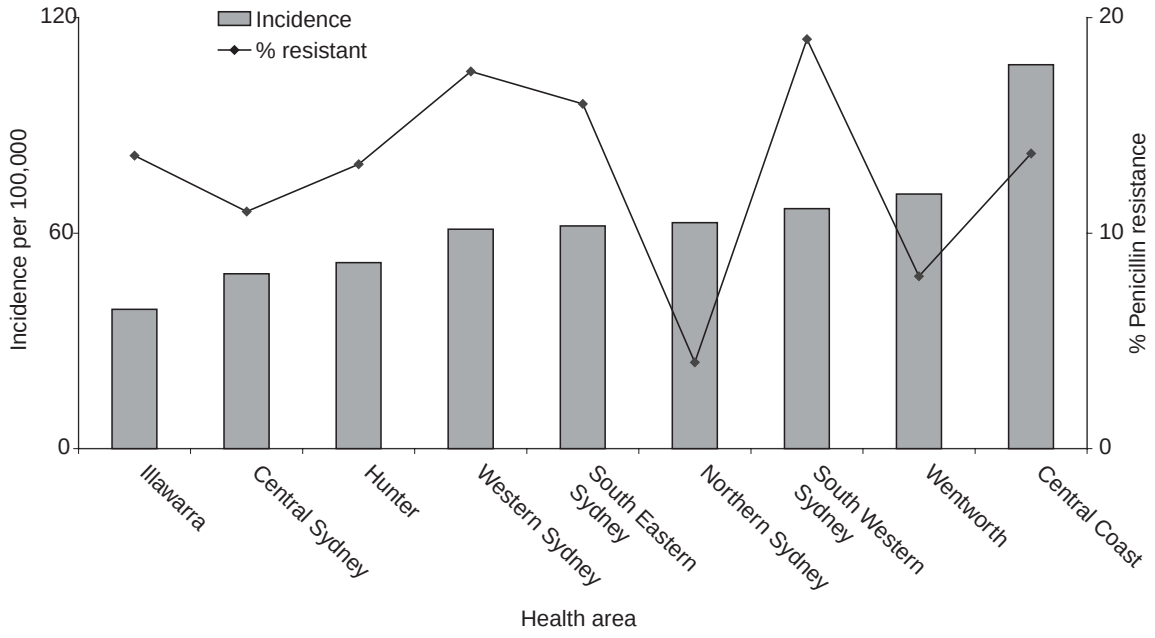
INCIDENCE OF INVASIVE PNEUMOCOCCAL DISEASE AND PREVALENCE OF PENICILLIN RESISTANCE FOR ALL AGES, METROPOLITAN NSW, 1997–2001



Source: The Metropolitan NSW Pneumococcal Study.

FIGURE 2

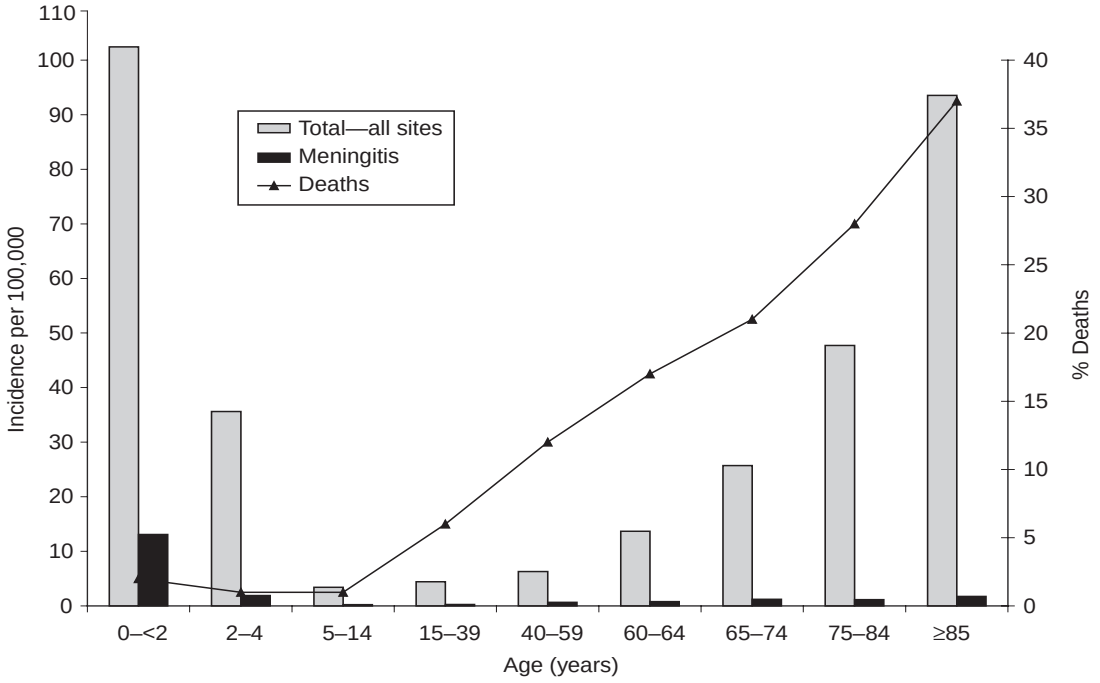
INCIDENCE OF INVASIVE PNEUMOCOCCAL DISEASE AND PREVALENCE OF PENICILLIN RESISTANCE FOR CHILDREN AGED LESS THAN FIVE YEARS, METROPOLITAN NSW, 1997–2001



Source: The Metropolitan NSW Pneumococcal Study.

FIGURE 3

AGE-SPECIFIC INCIDENCE AND MORTALITY FOR INVASIVE PNEUMOCOCCAL DISEASE, METROPOLITAN NSW, FOR ALL SITES AND FOR MENINGITIS ALONE, 1997–2001



Source: The Metropolitan NSW Pneumococcal Study.

15–64 years, and 20/118 (17 per cent) in those 65 years and over. In those with underlying illness, the corresponding figures were 7/168 (four per cent) in those 0–14 years, 76/551 (14 per cent) in those 15–64 years, and 288/979 (29 per cent) in those 65 years and over.

DISCUSSION

These data from metropolitan health areas of NSW show a similar pattern to that demonstrated previously, with respect to age-specific incidence and pattern of infection, as well as the prevalence of underlying conditions and age-specific mortality.[2] The total annual incidence of disease in children aged 0–2 years increased slightly from 95.2 to 102.4 per 100,000, as did the incidence of meningitis (12.5 to 13.1 per 100,000). The seasonal distribution of cases—with a preponderance in the colder months of the year in temperate climates—is in keeping with previous reports.

The serogroup distribution of cases in this extended period of surveillance remained similar to that previously documented and to reports from North America,[1] and other areas of Australia,[2] which do not have large Indigenous populations. Interestingly, the level of penicillin resistance found in these sterile site pneumococcal isolates—higher than in many other areas of Australia in 1997—has declined overall. However, this report highlights the substantial variations in incidence and particularly in penicillin resistance, seen between regions covered by the metropolitan health areas. It should be noted, however, that standard methodology for testing penicillin resistance was not used and that re-testing of all isolates in the same laboratory may have resulted in some re-classification. This is unlikely to be of sufficient magnitude to alter the broad findings.

Are these observed differences real, or are they related to case ascertainment, as documented in South Carolina?[7] Higher burdens of pneumococcal disease have previously been shown to correlate with lower socioeconomic status,[8] although diagnostic practices, especially in indications for blood culture, may also account for some of the variation seen. This, however, is unlikely to account for differences in the prevalence of antibiotic resistance, which are more likely to be related to the introduction of certain antibiotic-resistant clones or to local patterns of antibiotic use.

Another important issue with respect to vaccination programs, both for 23-valent pneumococcal polysaccharide vaccine and 7-valent conjugate pneumococcal vaccine is the prevalence of predisposing conditions by age.[9] With respect to polysaccharide vaccine, most people in the over 65 years age group, for whom the vaccine is currently recommended, have at least one

predisposing medical condition and so should be under regular medical review. With respect to the current program of funded pneumococcal conjugate vaccine, which for non-Indigenous children includes only a restricted range of conditions, only a minority of children with IPD will be eligible.

CONCLUSION

These data provide an expanded picture of the profile of IPD in a representative Australian urban region—the metropolitan area health services within Sydney, the Hunter and the Illawarra. They are a useful baseline against which the effect of potential vaccination programs, both for polysaccharide vaccine in the elderly and conjugate vaccine in infants, can be evaluated prior to IPD becoming notifiable in NSW in 2001.

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